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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/986,750	11/09/2001	Richard M. Pires	0942.5080001 RWE FRC	5957

26111 7590 07/02/2002

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EXAMINER
SCHULTZ, JAMES

ART UNIT	PAPER NUMBER
1635	9

DATE MAILED: 07/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/986,750	Applicant(s) PIRES ET AL.
	Examiner James D. Schultz	Art Unit 1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Interview Summary (PTO-413) Paper No(s).

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kempe et al., in view of Lyttle et al.

The claims of the instant invention are drawn to a method of cleaving an oligonucleotide from a linker using a gaseous nucleophile, wherein the linker is a universal linker, or is not the 3'-terminal of the nucleotide, or the ester linkage between the 3'-OH of the oligo and the phosphate of the linker is cleaved, or wherein the linker contains a phosphorus containing heterocycle after cleavage, or wherein the linker contains 2 vicinal heteroatoms, or wherein the nucleophile is ammonia or hydrated ammonia vapors, or wherein cleavage may take place between 1 and 240, or room temperature and 150, or at 95 degrees Celsius, or wherein cleavage is substantial, or wherein said cleaved oligos are recovered by washing the solid phase in water or buffer, or wherein the oligo, linker and solid support has the formula as depicted in claim 19, or wherein X of the formula of claim 19 is the 3' terminal of the oligo, or wherein the protecting group of claim 19 has a specific composition.

Kempe et al. teaches a method of cleaving an oligonucleotide attached to a solid support via a linker arm (col. 1 line 26) using a gaseous nucleophile, wherein the nucleophile is ammonia or hydrated ammonia vapors, wherein cleavage may take place at 85 degrees Celsius, or wherein

said cleaved oligos are recovered by washing the solid phase in water or buffer. Kempe does not teach using universal linker comprising vicinal heteroatoms, or teach a conjugate comprising an oligo, linker and solid support with the formula as depicted in claim 19 of the instant application, wherein X of the formula of claim 19 is the 3' terminal of the oligo, or wherein the protecting group of claim 19 has a specific composition.

Lyttle et al. teaches using ammonia as a nucleophile to cleave an oligo from a universal linker wherein the 3'-terminal of the nucleotide or the ester linkage between the 3'-OH of the oligo and the phosphate of the linker is cleaved, or wherein the linker contains a phosphorus containing heterocycle after cleavage, or wherein the linker contains 2 vicinal heteroatoms, or wherein the nucleophile is ammonia, wherein the linker is one comprising vicinal heteroatoms. Lyttle et al. also teaches a conjugate comprising an oligo, linker and solid support with the formula substantially as depicted in claim 19 of the instant application, wherein X of the formula of claim 19 is the 3' terminal of the oligo, or wherein the protecting group of claim 19 is an acyl group.

It would have been obvious to one of ordinary skill in the art to employ the cleavage protocol using the gaseous nucleophile ammonia as taught by Kempe et al. with the vicinal heteroatom containing linkers as taught by Lyttle et al. One of ordinary skill in the art would have been motivated to do so because Lyttle et al. teach that the use of such universal linkers expedites oligo synthesis by facilitating easier use of multiple well plates (Intro., line 6), and since Kempe et al. teach that use of a gaseous nucleophilic ammonia enhances efficacy by significantly reducing the time required for recovery of synthesized oligonucleotides. Additionally, one or ordinary skill in the art would have had a reasonable expectation of success

in using the gaseous nucleophile-mediated cleavage of Kempe et al. to cleave the oligos from the linkers of Lyttle et al., because Lyttle et al. already teach the use of ammonia as a nucleophile for cleavage, and since Kempe et al. had previously demonstrated that use ammonia in the gaseous phase hastened the recovery of synthesized oligonucleotides as compared to aqueous ammonia, without changing its inherent ability to act as a nucleophile during cleavage.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Schultz whose telephone number is 703-308-9355. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 703-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

James D. Schultz, PhD
June 25, 2002

ANDREW WANG
PRIMARY EXAMINER